

Remarks/Arguments:

The specification (page 5, 1st complete ¶) is amended to contain the address of the depository.

Claims 20-23, currently amended, and claims 24, 25, and 27-30, previously presented, are pending.

Claims 1-19, 26, and 31-60 are cancelled, without prejudice or disclaimer.

Claim 20 is amended, hereby, by deleting subject matter relating to "SEQ ID NO: 1"; accordingly, the nucleic acid of claim 20 (currently amended) is one of:

- SEQ ID NO: 2 or its complimentary sequence,
- a fragment of SEQ ID NO: 2, or
- a sequence derived from SEQ ID NO: 2 by mutation, deletion, and/or substitution of one or more bases.

Both of claims 20 and 21 are amended, hereby, by deleting the term "specifically" and, further, by replacing "high stringency conditions" with

contacting with a hybridization solution of 5-fold concentrated sodium saline phosphate EDTA, 0.5% Tween 20, and 0.01% merthiolate followed by washing with a solution containing 10 mM Tris-HCl, 300 mM NaCl and 0.1% Tween 20, pH 7.4,

i.e., the high stringency conditions disclosed in the specification at page 15, lines 33-36, and page 16, lines 6-7. A copy of *Molecular Cloning*, 3, 1989, Annex B, 13 (referenced at specification page 13, lines 33-34) is attached to this paper. The attached reference demonstrates that composition of the SSPE buffer—the "sodium saline phosphate EDTA"—was known to those skilled in the art. Applicants wish to point out that the subject application does not describe these high stringency

conditions in association with a specific nucleic acid sequence; rather, they are described as allowing detection of nucleic acids from *E. coli* O157:H7 or other EHECs.

Claim 21 is amended, hereby, by deleting subject matter relating to "mutation." Thus, the nucleic acid of claim 21 (currently amended) is limited to one of

- SEQ ID NO: 1,
- a fragment of SEQ ID NO: 1, or
- a sequence derived from SEQ ID NO: 1 by deletion and/or substitution of one or more bases.

Claim 21 is also amended by limiting the "fragment of" and "sequence derived from" SEQ ID NO: 1 such that each "detects an *Escherichia coli* as being enterohaemorrhagic *Escherichia coli* . . . (EHEC) of serotype O157:H7." As described in the specification (page 5, lines 13-19), the stable combination of a portion of the insertion sequence IS91 and of the sequence katP found in SEQ ID NO: 1 is a hallmark of *E. coli* O157:H7.

Claim 22 is amended by limiting each of the alternatives

- fragment of SEQ ID NO: 1 and
- sequence derived from SEQ ID NO: 1

in claim 21—each already containing nucleotides 400-407 of SEQ ID NO: 1—to "a nucleotide chain of at least 10 consecutive nucleotides of SEQ ID NO: 1," i.e., as supported by the specification, page 7, line 38, to page 8, line 3.

Applicants wish to thank the Examiner for reconsidering the restriction requirement and, accordingly, rejoining invention Groups I-III, as requested. The remainder of the restriction requirement is rendered moot by cancellation, hereby, of withdrawn claims 31-60.

Claims 20 and 21 were rejected under 35 USC 112, first paragraph, for allegedly failing to satisfy the written description requirement, i.e., with respect to the "sequence derived from SEQ ID NO: 2" (claim 20) and the "sequence derived from SEQ ID NO: 1" (claim 21) . Reconsideration is requested.

First of all, there is adequate literal support in the specification for each of the recited "derived" sequences. Secondly, the claims require that the derived sequence must "hybridize," under the recited stringency conditions, with either SEQ ID NO: 2 or its complementary sequence (claim 20) or SEQ ID NO: 1 or its complementary sequence (claim 21) .

Moreover, as regards claim 21—and SEQ ID NO: 1—the derived sequence further contains nucleotide chain of SEQ ID NO: 1 that encompasses the junction resulting from the insertion of IS91 into katP gene.

The presently claimed invention critically relies on the demonstration that EHECs are identified by detecting a nucleic acid of sequence SEQ ID NO: 2 (claim 20) and the EHEC of serotype O157:H7 is identified by detecting a nucleic acid of sequence SEQ ID NO: 1 (claim 20).

Accordingly, it would have been reasonable for one skilled in the art to conclude that, at the time of the instant invention, the inventors had possession of (1) nucleic acids derived from SEQ ID NO: 1 by deletion and/or substitution that, nevertheless, hybridized with SEQ ID NO: 1 (or its

complementary sequence) and (2) nucleic acids derived from SEQ ID NO: 2 by deletion and/or substitution that, nevertheless, hybridized with SEQ ID NO: 2 (or its complementary sequence).

Applicants submit that compliance with the written description requirement does not require that examples of such derived sequences be expressly described in the subject application.

Claims 20-25 are rejected under 35 USC 112, first paragraph, and the specification objected to under 35 USC 132(a), for allegedly containing new matter. Reconsideration is requested.

Contrary to the allegations set forth in the statement of rejection, the amendment to the specification does not rely for support on an error occurring in the English language translation of the international PCT application. On the contrary, as stated in the Amendment filed July 12, 2004 (page 4) (*emphasis added*):

In accordance with the "Sequence Listing" in the subject application, the oligonucleotides identified as SEQ ID NOS: 3 to 20 correspond to nucleotide sequences appearing in SEQ ID NO: 1. Also in accordance with the "Sequence Listing," the oligonucleotides identified as SEQ ID NOS: 21 to 27 correspond to nucleotide sequences appearing in SEQ ID NO: 2. Accordingly, the text as amended, hereby, reflects a correction that would have been readily apparent to one of ordinary skill in the art.

Accordingly, support for the amendment is found in the "Sequence Listing" of the originally filed application, itself. As readily apparent from the Sequence Listing, SEQ ID NOS: 21-27 are fragments of SEQ ID NO: 2, not SEQ ID NO: 1.

The PTO considered that the term "specifically" introduced in claims 20 and 21 added new matter. This issue is rendered moot as "specifically" is deleted from the claims, hereby, as indicated above.

In view of the foregoing explanation, withdrawal of the new matter rejection under §112, ¶1, and objection under §132(a) are apparently in order.

Claims 20-25 were rejected under 35 USC 112, first paragraph, for allegedly lacking enablement. Reconsideration is requested.

Lack of enablement is alleged with respect to previously amending the claims so that both the "fragment" and the "derived sequence"—of SEQ ID NOS: 1 and 2—"specifically detects enterohaemorrhagic *Escherichia coli*." Since the previously added "specifically" is deleted from the claims, hereby, the rejection is rendered moot. Correspondingly, withdrawal of the rejection under §112, ¶1, for alleged lack of enablement appears to be in order.

Claims 20-25 were rejected under 35 USC 112, second paragraph, as allegedly being indefinite for reciting "under stringent conditions." Reconsideration is requested.

As explained, above, the high stringency conditions disclosed in the specification at page 15, lines 33-36, and page 16, lines 6-7, are inserted into the claims in place of the phrase "under stringent conditions." Accordingly, the allegedly indefinite language being deleted from the claims, hereby, withdrawal of the corresponding rejection under §112, ¶2, appears to be in order.

Claims 20-25 stand rejected under 35 USC 112, second paragraph, as allegedly being indefinite for reciting "specifically detects." Reconsideration is requested.

As explained, above, the previously added modifier "specifically" is deleted from the claims, hereby. As such, the corresponding §112, ¶2, rejection is rendered moot and, correspondingly, withdrawal of the rejection appears to be in order.

Claims 20, 21, 22 and 24 were rejected under 35 USC 102(b) as being allegedly anticipated by *Microbiology, 146, 3305-3315, 1996* (Brunder) reconsideration is requested.

Claim 20 has been limited to SEQ ID NO: 2 or its complementary sequence, a fragment thereof, and a sequence derived therefrom. Hence, claim 20 (currently amended) is clearly novel over Brunder, as the subject matter allegedly found in the reference has been deleted from the claim.

As regards claim 21, the claimed nucleic acid consists of:

- SEQ ID NO: 1 or fragment thereof that contains a nucleotide chain of SEQ ID NO: 1 resulting from stable combination of at least a portion of insertion sequence IS91 and at least a portion of gene sequence katP or
- a sequence derived by deletion and/or substitutions from SEQ ID NO: 1, hybridizing with SEQ ID NO: 1 or its complementary sequence under the recited hybridization conditions and containing a nucleotide chain of SEQ ID NO: 1 resulting from stable combination of at least a portion of insertion sequence IS91 and at least a portion of gene sequence katP.

Thus, contrary to the PTO's assertion, the specific junction of 1591 and katP is defined in claim 21 through the explicit reference to the "nucleotide chain of SEQ ID NO: 1." It is readily apparent from Figure 1 (SEQ ID NO: 1) that the junction of a portion of IS91 and a portion of katP is found at positions 406 (3' end of the inserted portion of IS91) and 407 (interrupted katP sequence).

According to claim 21, the claimed derived sequences have to contain an unaltered nucleotide chain of SEQ 1D NO: 1, which contains the nucleotides in positions 406/407.

Additionally, the PTO's definition for "substitution" is based on speculation—no evidentiary support is provided. Moreover, the PTO definition for this term is contrary to the art-accepted definition. For example, the attached page from www.web-books.com defines "substitution" as "one or more nucleotides . . . substituted by *the same number* of different nucleotides" (*emphasis added*). In no way can "substitution" be defined as replacement of a number of nucleotides by a *different* number of nucleotides, as alleged in the statement of rejection. The definition of a claim limitation given by the PTO cannot be different than would be given by one of ordinary skill in the art. *In re Cortright*, 49 USPQ2d 1464 (Fed. Cir. 1999).

Hence, the nucleic acid of present claim 21—"consisting of nucleotide sequence SEQ ID NO: 1, a fragment thereof, or a sequence derived from SEQ ID NO: 1 by deletion and/or substitution of one or more bases"—can be no longer than the length of SEQ ID NO: 1, i.e., it has a maximum sequence length of 1489 base pairs. Plasmid pSml0, according to Brunder (page 3306, right column, last sentence of first paragraph) is prepared by cloning a 9.7 kb SmaI fragment from p0157 in phagemid vector pBluescript IIKS. Therefore, plasmid pSml0 is clearly outside the scope of present claim 21.

Accordingly, for the foregoing reasons, withdrawal of the rejection under § 102(b) based on Brunder appears to be in order.

Claims 20, 21, 22, 24 and 25 were rejected under 35 USC 102(b) as being allegedly anticipated by *DNA Research*, 5, 1-9, 1998 (Makino) in view of GenEMBL Accession No. AB011549. Reconsideration is requested.

First of all, the §102(b) rejection cannot be maintained because it relies on more than one reference. *Structural Rubber v. Park Rubber*, 223 USPQ 1264 (Fed. Cir. 1984). A second reference cannot be used to expand the meaning of a (1st) reference that allegedly anticipates the claims in a rejection under §102(b). *In re Baxter Travenol Labs*, 21 USPQ2d 1281, 1284 (Fed. Cir. 1991).

As implicitly acknowledged by the PTO, applicants are not claiming plasmid pO157 disclosed in Makino. The PTO alleges that plasmid pO157 contains segments corresponding to each of SEQ ID NO:1 and SEQ ID NO:2, e.g., plasmid pO157 allegedly "comprises a sequence that is 98.7% identical as compared to SEQ ID NO:2 as evidenced by GenEMBL Accession No. AB011549" (Office Action, paragraph bridging pages 6 and 7). Accordingly, knowledge of the sequence of plasmid pO157 would have been indispensable in determining the "sequence that is 98.7% identical as compared to SEQ ID NO:2."

However, Makino does not disclose the sequence of plasmid pO157; the reference merely discloses that the sequence for pO157 "will appear in the DDBJ/EMBL/GenBank nucleotide sequence data basis with Accession Nos. AB011548" (Makino, page 2, §2.4) (*emphasis added*). Interestingly, the PTO fails to indicate a publication date, i.e., effective date as prior art under §102(b), for GenEMBL Accession No. AB011549. However, the face of the document, itself, states: "On Apr. [sic] 20, 1999[,] this sequence version replaced gi:3336997." In other words, the sequence "version" relied on by the PTO in order to reject the claims has an effective date as prior art under §102(b), at the very earliest, of April 20, 1999, which is less than one year before the actual filing date of the subject application, i.e., April 27, 1999 (the filing date of the §371 international

application) and, therefore, is not prior art under §102(b). What is more, applicants' §119(a) priority date (April 28, 1998) antedates the effective prior art date of GenEMBL Accession No. AB011549 by almost one year.

Applicants note that the PTO relies on the alleged fact that Makino is *enabling* with respect to plasmid pO157. Even assuming, arguendo, that the PTO were correct in this respect, it is not pertinent to the issue at hand. It must be remembered that applicants are not claiming plasmid pO157 and, so, even assuming that Makino put the public in possession of plasmid pO157, nothing in the reference teaches or suggests a fragment of the plasmid that corresponds to either SEQ ID NO:1 or SEQ ID NO:2. For example, nothing in Makino teaches or suggests the "sequence" within plasmid pO157 "that is 98.7% identical as compared to SEQ ID NO:2," allegations to the contrary in the statement of rejection, notwithstanding. Since Makino does not put the public in possession of the identical invention claimed, it can not anticipate the presently claimed invention. *In re Donahue*, 226 USPQ 619 (Fed. Cir. 1985).

As also previously explained of record, Makino teaches that plasmid O157—obtained (isolated) from *E. coli* O157:H7—contains 1860 open reading frames (ORFs). This 1860-ORF plasmid does not anticipate a 186 ORF nucleic acid *fragment* of the plasmid—i.e., a claimed nucleic acid "consisting of" the 186 ORFs. A reference that discloses "substantially the same invention" is not an anticipation. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 USPQ 253 (Fed. Cir. 1985). To be novelty defeating, a reference must put the public in possession of the identical invention claimed. *Donahue, supra*.

The plasmid disclosed by Makino does not fall within the scope of the present claims, which is limited to the nucleic acid "consisting of either " SEQ ID NO: 1 or SEQ ID NO:2, its complementary sequence, a fragment of the sequence, or the sequence modified by mutation (SEQ ID NO:2, only), deletion, and/or substitution, all of which are no longer than either SEQ ID NO: 1 or SEQ ID NO:2.

Accordingly, for the foregoing reasons the rejection for alleged anticipation, under §102(b), by Makino in view of GenEMBL Accession No. AB011549 appears to be in order for withdrawal.

Claims 20-25 stand rejected under 35 USC 103(a) as being allegedly unpatentable over Makino in view of *Microbiology*, 142, 907-914, 1996 (Schmidt) and *Progr. Nucl. Acid Res. Mole. Biol.* 11, 259-301, 1971 (Kennell) and further in view of GenEMBL Accession No. AB011549. Reconsideration is requested.

The rejection under §103(a) fails for the same reasons that the rejection under §102(b) based on Makino in view of GenEMBL Accession No. AB011549 fails, as explained above. Neither Schmidt nor Kennell — taken alone or together — adds any disclosure that cures the fatal deficiencies of Makino in view of GenEMBL Accession No. AB011549 in meeting all limitations on the present claims. All limitations on the present claims not being supported by the cited references, the rejection under §103(a) is " inadequate on its face." *In re Thrift*, 63 USPQ2d 2002, 2008 (Fed. Cir. 2002), and withdrawal of the rejection appears to be in order.

Request to Withdraw Premature Final Rejection

Request is made, hereby, for reconsideration and withdrawal of the "Final" Office Action, mailed April 15, 2002 ("the Office Action"), and for a new, non-final action in place of the Final action, which new action restarts the time period for response. As explained, below, withdrawing finality of the Office Action is required, in accordance with MPEP 706.07(a) and 706.07(d), because the Office Action contains a "new ground of rejection," not necessitated by applicant amendment, which renders the finality "premature."

Where finality of an Office Action is "premature," the "finality of the Office Action must be withdrawn." MPEP 706.07(d). A final Office Action is "premature," for purposes of MPEP 706.07(d),

where the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(C) with the fee set forth in 37 CFR 1.17(p). MPEP 706.07(a).

The final Office Action contains a new grounds of rejection under 35 U.S.C. 103(a) based on Ayer, alone. The new grounds of rejection is applied against only claims 117-121, as being product-by-process claims, i.e., process steps being allegedly unentitled to any patentable weight in a product claim (final Office Action, §4, page 4). According to the final Office Action (page 7), the new grounds of rejection was necessitated by Applicants' previously filed Amendment, but this is incorrect.

A rejection is "new" under standards of the controlling case law.

The criterion of whether a rejection is considered new" is whether the applicant "had a fair opportunity to react to the thrust of the rejection. *In re Kronig*, 190 USPQ 425 (CCPA 1976).

Ex parte Maas, 14 USPQ2d 1762, 1764 (BPA&I 1990). In the present situation, Applicants had no "fair opportunity to react to the thrust of the rejection" at issue, since no such rejection was previously made of record.

Rejected product-by-process claim 117 represents previously examined product-by-process claims 41 and 78. In fact, product-by-process claim 41 was not only previously examined, it had been found "allowable if rewritten in independent form" (Office Action mailed December 28, 2000, page 3). Accordingly, statements to the contrary in the final Office Action, notwithstanding, since the new grounds of rejection was in no way "necessitated by applicant's amendment," finality of the final Office Action was "premature." MPEP 706.07(a). Being "premature," the "finality of the Office action must be withdrawn." MPEP 706.07(d).

For the foregoing reasons, the final action introduced a new ground of rejection, which was premature, and which, thus, requires withdrawal of the final action. MPEP §§ 706.07(a), 706.07(d). Accordingly, a new non-final Office Action is in order to be issued by the PTO, in place of the final action, which new action resets the time period for response as of its mailing date.

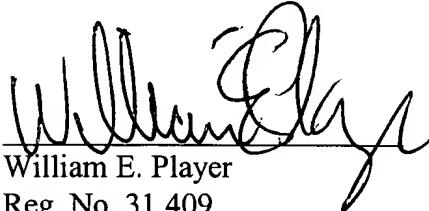
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Favorable action is requested.

Respectfully submitted,

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